A randomized, comparative study to evaluate the efficacy and tolerability of a 3-day course of azithromycin versus a 10-day course of co-amoxiclav as treatment of adult patients with lower respiratory tract infections

J. Zachariah

*ICON Clinical Research Ltd, Dundrum Castle, Ballinteer Road, Dublin, Ireland*

Clinical and bacteriological efficacy and tolerability of azithromycin (500 mg once daily for 3 days) and those of a 10-day regimen of co-amoxiclav (37 mg three times daily) were evaluated in a large-scale, double-blind comparative study of 369 patients (≥18 years old) with acute lower respiratory tract infections. After treatment, 165/173 (95%) azithromycin- and 166/173 (96%) co-amoxiclav-treated patients had responded satisfactorily (cure or improvement). Baseline pathogens (mainly *Streptococcus pneumoniae* and *Haemophilus influenzae*) were eradicated in 82/82 (100%) azithromycin- and 73/74 (99%) co-amoxiclav-treated patients who were bacteriologically assessable. Adverse events, which were predominantly of mild to moderate severity and mostly affected the gastrointestinal system, were recorded in 13/186 (7%) azithromycin- and 19/183 (10%) co-amoxiclav-treated patients. Only two (1%) azithromycin-treated patients discontinued treatment due to adverse events compared with eight (4%) who received co-amoxiclav. The results show that azithromycin at a dose of 500 mg once daily for 3 days is an effective and safe alternative to a 10-day, three-times-daily course of co-amoxiclav in the treatment of lower respiratory tract infections in adults.

Introduction

Worldwide, lower respiratory tract infections are a major health concern not only because of their associated morbidity and mortality, but also because of their cost to the community (Krosick, 1991). Although many of these infections are of viral origin, a large proportion are of bacterial aetiology or are bacterial superinfections of viral infections. *Streptococcus pneumoniae*, *Haemophilus influenzae* and *Moraxella catarrhalis* are among the most important bacterial pathogens, and *Staphylococcus aureus* also plays an important role.

For the last four decades, orally-administered penicillins have been widely used in the treatment of lower respiratory tract infections, but as the end of the century approaches new difficulties have arisen which are curbing the use of these classic antimicrobial agents. One of the most pressing is the emergence of penicillin-resistant strains of *S. pneumoniae* and amoxycillin/ampicillin-resistant strains of *H. influenzae* and *M. catarrhalis*. Where resistance is due to β-lactamase production, as in most strains of *M. catarrhalis* and many strains of *H. influenzae* and *S. aureus*, the addition of a β-lactamase-inhibitor (e.g. clavulanic acid or sulbactam) has overcome the problem.
Amoxycillin plus clavulanic acid (co-amoxiclav) is one such penicillin plus β-lactamase inhibitor formulation and is widely used for respiratory tract infections. Amoxycillin has the best activity of the oral penicillins against pneumococci, whether these have high- or low-level resistance, provided the number of resistant strains in the population is low. Resistance is also, however, mediated by mechanisms other than β-lactamase production and where the pathogen is an amoxycillin-resistant, β-lactamase-negative *H. influenzae* or *S. aureus* strain addition of a β-lactamase inhibitor fails to alleviate resistance to the penicillin. Penicillins also have a disadvantage because of the need for a 7–10-day course of treatment with multiple-daily dosing; this may give rise to poor treatment compliance. Furthermore, hypersensitivity to penicillins may be problem.

A 10-day course of the macrolide erythromycin has often been used as an alternative to penicillin when there are problems of hypersensitivity to penicillins, or where microbial resistance to penicillin has led to treatment failure. However, the high incidence of gastrointestinal side-effects associated with erythromycin (Pilot & Qin, 1988; Pechère, 1993), its unreliable absorption following oral administration and its low activity against *H. influenzae* have limited its use. Furthermore, in common with the penicillins, erythromycin's multiple-daily dose regimen may result in poor compliance with detrimental effects on treatment outcome (Greenberg, 1984; Cockburn et al., 1987).

An alternative to erythromycin is the azalide azithromycin, which although structurally similar to erythromycin, has a methyl-substituted nitrogen at position 9a of the lactone ring (Bright et al., 1988). This structural modification results in azithromycin's greater bioavailability after oral administration compared with erythromycin (Fiese & Steffen, 1990) and improved activity against *H. influenzae* (Retsema et al., 1987). Azithromycin's activity against the respiratory pathogens *S. pneumoniae* (MIC<sub>90</sub> 0.05–0.12 mg/L) and *M. catarrhalis* (MIC<sub>90</sub> 0.03 mg/L) is also excellent (Retsema et al., 1987; Hardy et al., 1988). Important pharmacokinetic features of azithromycin are its ability to penetrate tissues rapidly and to maintain tissue concentrations in excess of those in serum for prolonged periods (Foulds, Shepard & Johnson, 1990). Among the tissues that azithromycin penetrates are the lungs and Baldwin et al. (1990) have demonstrated high levels of the azalide in bronchial mucosa, epithelial lining fluid and sputum. Azithromycin is also able to target infected tissue. The antimicrobial agent is actively transported to sites of infections by phagocytic cells and thereafter is released in response to stimuli from the pathogens themselves (Panteix et al., 1993; Retsema et al., 1993).

Extrapolation of pharmacokinetic and bacteriological data indicates that a 3-day, once-daily regimen of azithromycin would be effective in the treatment of lower respiratory tract infections, and small-scale studies have demonstrated that such a regimen is as effective as a 10-day course of co-amoxiclav (Hoepelman et al., 1993; Sevieri, Roggi & Monacci, 1993). The present study was carried out to confirm this finding and to compare the tolerance of the two regimens.

**Patients and methods**

**Patient enrolment**

Adults (i.e. ≥ 18 years old) of either sex, diagnosed as suffering from acute bronchitis, acute infectious exacerbations of chronic bronchitis (AIECBs), or community-acquired pneumonia, were eligible for inclusion in the study. Acute bronchitis was defined as the
Treatment of LRTI

presence of purulent sputum together with fever (≥38°C), leucocytosis (≥10 x 10⁹/L) and/or symptoms suggestive of lower respiratory tract infection. Patients were considered to have chronic bronchitis if they had a history of chronic or recurrent productive cough present on most days for at least 3 months for a minimum of 2 years and acute exacerbations were defined in terms of symptoms, as described by Anthonisen et al. (1987). A diagnosis of pneumonia was made if a patient had signs and symptoms of a lower respiratory tract infection, similar to those of acute bronchitis, a chest X-ray showed a new pulmonary infiltrate and also had a productive cough, purulent sputum (<10 epithelial cells per low-power field and ≥25 polymorphonuclear leucocytes per high-power field), a positive sputum culture, a fever of ≥38°C recorded twice or more within a 24-h period and/or an increased WBC (10 x 10⁹/L). Pneumonia in patients >75 years old was excluded from the study, as were those with consolidation of more than one entire lung lobe, with a WBC of 30 x 10⁹/L or more, who required oxygen, or who were bacteraemic.

All women of child-bearing potential had to be using adequate contraception in order to be included; women who were pregnant or breast-feeding were excluded. Other reasons for exclusion of a patient were a terminal illness or condition that would preclude study completion, a gastrointestinal condition that could affect drug absorption, a hepatic disorder in which serum aminotransferase levels were threefold higher than the normal upper limit, or infectious mononucleosis. Also, patients were excluded if they were receiving concomitant ergotamine, cyclosporin, antacid (except H₂-antagonists) or digitalis glycoside therapy, or if they were known to be hypersensitive to either macrolide or β-lactam antimicrobial agents. No patients were enrolled in the study if they had a concurrent infection that required treatment with another antimicrobial agent, or if the Gram stain indicated that the infection was one for which either of the study drugs was inappropriate. Patients who had received another antimicrobial agent in the previous 2 weeks were only included if there was bacteriological evidence that the previous treatment had been ineffective. Dependency on drugs or alcohol also excluded patients from participation in this study.

Study design

Appropriate institutional review board approval was obtained and the study was performed in accordance with this. All patients provided written informed consent before inclusion in the study.

After enrolment, patients were randomly assigned to one of the treatment groups and received the following therapy: azithromycin (Pfizer), one 500 mg tablet once daily for 3 days; or co-amoxiclav (Augmentin; Smithkline Beecham), one 375 mg tablet three times daily for 10 days. Matched placebo tablets were employed to maintain blinding of the study: azithromycin group patients received placebo ‘co-amoxiclav’ tablets three times daily for 10 days and co-amoxiclav patients received placebo ‘azithromycin’ tablets for 3 days.

Clinical signs and symptoms were recorded before the start of treatment on day 1. Patients were also assessed clinically on days 5 ± 2 and 14 ± 2, and changes noted. At the day 14 ± 2 assessment, patients were classified as cured, improved, failed, or relapsed (Table I). Those patients who were considered to have improved at the end of therapy (day 14 ± 2) were followed up on day 21 ± 2. Only the final clinical response (i.e. on day 14, or day 21) is presented in the tables.
Sputum samples were obtained before therapy and, where possible, after completion of treatment. Organisms were cultured and then identified. A disc diffusion method employing Mueller-Hinton agar was used to test susceptibility (National Committee on Clinical Laboratory Standards, 1985). Pathogens were considered to be susceptible to azithromycin if they had an MIC $< 2$ mg/L, of intermediate susceptibility if the MIC was 4 mg/L and resistant if the MIC was $\geq 8$ mg/L (Barry & Jones, 1988; Barry, Jones & Thornsberry, 1988; Barry et al., 1989). Those patients without purulent sputum before the start of treatment were only assessed clinically.

Bacteriological response was recorded at the end of therapy (day 14 ± 2) and was categorized as eradication or persistence (Table I). If no sputum sample was obtainable as a result of resolution of cough, the pathogen was assumed to be eradicated.

At assessments performed on days 5 ± 2 and 14 ± 2, any adverse events reported spontaneously or observed by the investigator were noted and classified as mild, moderate, or severe. The event's relationship to treatment (related, not related, or uncertain/unknown) was also recorded.

Blood and urine samples were obtained from all patients on entry to the study and on day 14 ± 2. Laboratory safety tests were performed and, if any abnormality in haematology, blood chemistry, or urinalysis was detected, the patient was monitored until the variable had returned to its value at baseline, or to within the normal range.

**Statistical analysis**

The Cochran-Mantel-Haenszel test based on Ridit scores was employed to compare clinical responses between the two treatment groups. Safety data for the two groups were compared using the $\chi^2$ or Fisher's exact test as appropriate. The statistical tests were all two-tailed and were performed at the 0.05 significance level.

<table>
<thead>
<tr>
<th>Table I. Definitions of clinical and bacteriological response</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Clinical response</strong></td>
</tr>
<tr>
<td>Cured</td>
</tr>
<tr>
<td>Improved</td>
</tr>
<tr>
<td>Failed</td>
</tr>
<tr>
<td>Relapsed</td>
</tr>
<tr>
<td><strong>Bacteriological response</strong></td>
</tr>
<tr>
<td>Eradication</td>
</tr>
<tr>
<td>Persistence</td>
</tr>
</tbody>
</table>
Table II. Baseline demographic characteristics of patients by treatment group

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Azithromycin (n = 186)</th>
<th>Co-amoxiclav (n = 183)</th>
</tr>
</thead>
<tbody>
<tr>
<td>No. of patients</td>
<td></td>
<td></td>
</tr>
<tr>
<td>male</td>
<td>94</td>
<td>95</td>
</tr>
<tr>
<td>female</td>
<td>92</td>
<td>88</td>
</tr>
<tr>
<td>Age (years)</td>
<td>mean ± S.D.</td>
<td>mean ± S.D.</td>
</tr>
<tr>
<td></td>
<td>55.9 ± 17.6</td>
<td>53.2 ± 18.1</td>
</tr>
<tr>
<td>range</td>
<td>19.8-92.6</td>
<td>14.8-91.8</td>
</tr>
<tr>
<td>Weight (kg)</td>
<td>mean ± S.D.</td>
<td>mean ± S.D.</td>
</tr>
<tr>
<td></td>
<td>71.1* ± 13.8</td>
<td>71.3 ± 12.9</td>
</tr>
<tr>
<td>range</td>
<td>29.0-121.5</td>
<td>42.0-114.8</td>
</tr>
<tr>
<td>Diagnosis</td>
<td></td>
<td></td>
</tr>
<tr>
<td>acute bronchitis</td>
<td>125</td>
<td>123</td>
</tr>
<tr>
<td>AIECB</td>
<td>60</td>
<td>59</td>
</tr>
<tr>
<td>pneumonia</td>
<td>1</td>
<td>1</td>
</tr>
</tbody>
</table>

AIECB, Acute infectious exacerbation of chronic bronchitis. *Weight not recorded for one female patient.

Results

A total of 369 patients (189 males, 180 females), between the ages of 14 and 93 years were enrolled by 13 investigators from Great Britain and 15 in Ireland, at 23 centres and were randomized to the azithromycin (n = 186) or the co-amoxiclav treatment group (n = 183). The two treatment groups were comparable in terms of distribution of the sexes, age, mean body weight and diagnoses (Table II). The commonest diagnosis in both treatment groups was acute bronchitis, occurring twice as frequently as AIECBs.

Clinical outcome

In the azithromycin group, 13 patients were excluded from the clinical efficacy analysis as were ten from the co-amoxiclav group. Reasons for exclusion were as follows: failure to meet entry criteria (four azithromycin and one co-amoxiclav-treated patients); protocol violation (two azithromycin-treated patients); lost to follow-up (three patients in each treatment group), adverse events (three azithromycin- and six co-amoxiclav-treated patients); and withdrawal from study (one azithromycin-treated patient). All except one of the azithromycin patients excluded from the clinical efficacy analysis had acute bronchitis; the remaining patient had AIECB. Of the ten non-evaluable patients assigned to receive co-amoxiclav, eight had acute bronchitis and two AIECBs.

Satisfactory clinical responses (cured or improved) were recorded in 165/173 (95%) patients treated with azithromycin and in 166/173 (96%) who received co-amoxiclav. Among the 228 patients with acute bronchitis who were clinically evaluable (azithromycin, 113; co-amoxiclav, 115), 109 (96%) azithromycin-treated patients and 112 (97%) who received co-amoxiclav were classified as responding satisfactorily (Table III). Of the remaining patients, four azithromycin-treated patients and two patients who received co-amoxiclav were deemed to be clinical failures, and one patient in the co-amoxiclav group relapsed. Of the patients with AIECBs, 59 receiving azithromycin and 57 patients in the co-amoxiclav group were clinically evaluable. The
clinical response was classed as satisfactory in 94% and 93% of patients in the respective treatment groups (Table III). Two (3%) azithromycin- and three (5%) co-amoxiclav-treated patients were classified as treatment failures, and two (3%) patients in the azithromycin and one (2%) in the co-amoxiclav group were considered to have relapsed. One patient in each treatment group was diagnosed as having pneumonia; both patients were clinically cured following treatment.

**Bacteriological outcome**

A total of 105 patients assigned to azithromycin treatment and 109 patients in the co-amoxiclav group were excluded from bacteriological evaluation; no baseline pathogen could be isolated for the majority of these patients (96, azithromycin group; 97, co-amoxiclav group). Pathogens considered to be resistant to the study drugs were isolated from four patients assigned to azithromycin treatment and from five in the co-amoxiclav group. Other non-evaluable patients had no follow-up culture.

Overall, the baseline pathogen was eradicated in all 82 bacteriologically-assessable patients who received azithromycin and in 73/74 (99%) patients treated with co-amoxiclav. Baseline pathogens were isolated from 48 acute bronchitis patients treated with azithromycin: two were infected with *S. aureus*; 21 with *S. pneumoniae*; 15 with *H. influenzae*; seven with *M. catarrhalis*; and three with both *S. pneumoniae* and *H. influenzae*. Pathogens were eradicated at the end of therapy in all 48 patients, 46 of whom were regarded as clinically cured and the other two as improved (Table IV). In the co-amoxiclav group, 47 patients with acute bronchitis had baseline pathogens: three had *S. aureus*; 14 *S. pneumoniae*; 19 *H. influenzae*; eight *M. catarrhalis*; and three had both *S. pneumoniae* and *H. influenzae*. All pathogens were eradicated by the end

<table>
<thead>
<tr>
<th>Diagnosis/response</th>
<th>Azithromycin (n = 173)</th>
<th>Co-amoxiclav (n = 173)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Acute bronchitis</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cured</td>
<td>101 (89%)</td>
<td>105 (91%)</td>
</tr>
<tr>
<td>Improved</td>
<td>8 (7%)</td>
<td>7 (6%)</td>
</tr>
<tr>
<td>Failed</td>
<td>4 (4%)</td>
<td>2 (2%)</td>
</tr>
<tr>
<td>Relapsed</td>
<td>0</td>
<td>1 (1%)</td>
</tr>
<tr>
<td><strong>AIECB</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cured</td>
<td>47 (80%)</td>
<td>46 (81%)</td>
</tr>
<tr>
<td>Improved</td>
<td>8 (14%)</td>
<td>7 (12%)</td>
</tr>
<tr>
<td>Failed</td>
<td>2 (3%)</td>
<td>3 (5%)</td>
</tr>
<tr>
<td>Relapsed</td>
<td>2 (3%)</td>
<td>1 (2%)</td>
</tr>
<tr>
<td><strong>Pneumonia</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cured</td>
<td>1 (100%)</td>
<td>1 (100%)</td>
</tr>
</tbody>
</table>

AIECB, Acute infectious exacerbations of chronic bronchitis.

*Patients who were classed as improved on day 14 ± 2 were reassessed on day 21 ± 2; the final response is reported.*
Table IV. Incidence of bacteriological eradication at end of therapy assessment (day 14 ± 2) in patients with lower respiratory tract infections treated with azithromycin or co-amoxiclav

<table>
<thead>
<tr>
<th>Diagnosis/pathogen</th>
<th>Azithromycin (n = 82)</th>
<th>Co-amoxiclav (n = 74)</th>
</tr>
</thead>
<tbody>
<tr>
<td>S. aureus</td>
<td>2/2</td>
<td>3/3</td>
</tr>
<tr>
<td>S. pneumoniae</td>
<td>21/21</td>
<td>14/14</td>
</tr>
<tr>
<td>H. influenzae</td>
<td>15/15</td>
<td>19/19</td>
</tr>
<tr>
<td>M. catarrhalis</td>
<td>7/7</td>
<td>8/8</td>
</tr>
<tr>
<td>S. pneumoniae + H. influenzae</td>
<td>3/3</td>
<td>3/3</td>
</tr>
</tbody>
</table>

AIECB, Acute infectious exacerbation of chronic bronchitis.

of treatment, and 46 patients were considered to be clinically cured or improved (Table IV). One patient was deemed to have relapsed despite eradication of the baseline pathogen, *H. influenzae*. Pathogens were isolated from 34 patients with AIECBs who received azithromycin: 13 were infected with *S. pneumoniae*; 12 with *H. influenzae*; one with *Haemophilus parainfluenzae*; five with *M. catarrhalis*; one with *Streptococcus pyogenes*; and two with both *S. pneumoniae* and *H. influenzae*. All pathogens had been eradicated at the end of treatment and 32 of the patients showed clinical cure or improvement (Table IV). One patient whose *H. influenzae* had been eradicated was considered to have clinically relapsed. At baseline in the co-amoxiclav group, *S. aureus* was isolated from two AIECB patients, *S. pneumoniae* from eight, *H. influenzae* from five and *M. catarrhalis* from 11 patients. The pathogens were eradicated in 25 of the 26 (96%) patients, and all were considered to be clinically cured or improved (Table IV). *H. influenzae* persisted in one patient who, nevertheless, was considered to have improved clinically. Only one patient with pneumonia, from the co-amoxiclav group, was bacteriologically evaluable (Table III). This patient's baseline pathogen (*S. pneumoniae*) had been eradicated by the end of treatment.

Safety

A total of 17 adverse events related or possibly related to study treatment were experienced by 13 (7%) of the 186 patients who received azithromycin, compared with the 25 adverse events recorded in 19 (10%) patients treated with co-amoxiclav (Table V). The majority of events recorded in the azithromycin group affected the gastrointestinal system (12 events) and were generally of mild (47%) or moderate (24%)
Table V. Adverse events related or possibly related to study treatment in patients who received azithromycin or co-amoxiclav

<table>
<thead>
<tr>
<th>Adverse events</th>
<th>Azithromycin</th>
<th>Co-amoxiclav</th>
</tr>
</thead>
<tbody>
<tr>
<td>No. of patients evaluated</td>
<td>186</td>
<td>183</td>
</tr>
<tr>
<td>No. of patients with adverse events</td>
<td>13 (7%)</td>
<td>19 (10.4%)</td>
</tr>
</tbody>
</table>
| Gastrointestinal | \begin{tabular}{ll}
abdominal pain & 2 \\
diarrhoea & 2 \\
dyspepsia & 0 \\
nausea & 7 \\
vomiting & 1 \\
\end{tabular} | \begin{tabular}{ll}
& 0 \\
& 7 \\
& 1 \\
& 2 \\
& 0 \\
\end{tabular} |
| Central nervous system | \begin{tabular}{ll}
dizziness & 2 \\
headache & 1 \\
somnolence & 0 \\
\end{tabular} | \begin{tabular}{ll}
& 0 \\
& 1 \\
& 1 \\
\end{tabular} |
| Dermatological | \begin{tabular}{ll}
pruritus & 0 \\
rash & 0 \\
\end{tabular} | \begin{tabular}{ll}
& 1 \\
& 1 \\
& 1 \\
& 1 \\
& 1 \\
\end{tabular} |
| Other | \begin{tabular}{ll}
& 2 \\
& 11 \\
\end{tabular} | \begin{tabular}{ll}
& 17 \\
& 25 \\
\end{tabular} |

severity. Two azithromycin-treated patients (1%) discontinued treatment because of nausea, dizziness and/or headache. Gastrointestinal adverse events affected ten patients in the co-amoxiclav treatment group. Of the 25 events associated with co-amoxiclav, 32% were considered to be of mild and 48% of moderate severity. A total of eight patients (4%) discontinued treatment because of adverse events, including one or more of the following: diarrhoea, nausea, headache, somnolence, pruritus, rash, menorrhagia, asthenia, fatigue, pain.

Discussion

The present study has demonstrated that 500 mg azithromycin administered once daily for 3 days is as effective, both clinically and bacteriologically, as a 10-day course of co-amoxiclav given three times each day in the treatment of lower respiratory tract infections. Previous studies have shown that such a 3-day, once-daily, course of azithromycin is as effective as longer, more complex regimens of amoxicillin alone (Mertens et al., 1992), other macrolides (Bradbury, 1993; Morandini, 1993) and cephalosporins (Barsic et al., 1994) in the treatment of acute lower respiratory tract infections. Furthermore, this study also confirms the results of other smaller-scale studies (Hoepelman et al., 1993; Sevieri et al., 1993; Beghi et al., 1994) showing that three doses of azithromycin were as effective as 30 doses of co-amoxiclav for the treatment of acute infections of the lower respiratory tract.

Azithromycin was well tolerated in the present study. Within the azithromycin treatment group, the incidence of adverse events considered to related or possibly related to therapy was lower than in the co-amoxiclav-treated patients. In addition, fewer patients discontinued therapy prematurely in the azithromycin group because of adverse events. These findings were consistent with those in previous studies comparing
azithromycin and co-amoxiclav (Hoepelman et al., 1993; Sevieri et al., 1993) where there was also a lower proportion of azithromycin patients with adverse events.

Over 65% of the patients in this study were diagnosed as having acute bronchitis. This condition is regarded by many clinicians as being primarily of viral aetiology and, as a result, many recommend that treatment for acute bronchitis is symptomatic. There is, therefore, controversy over the role of antibiotic therapy (Gwaltney, 1990). In the current study, however, bacterial pathogens were isolated from 48/113 (42%) acute bronchitis patients in the azithromycin group and, 47/115 (42%) of patients assigned to co-amoxiclav. All pathogens were eradicated from these patients by the end of therapy. Furthermore, satisfactory clinical response rates were achieved in 96% and 97%, respectively, of azithromycin- and co-amoxiclav-treated patients, including those for whom no pathogens had been identified. This suggests antibacterial agents have an important role in first-line treatment of acute bronchitis, even when this has not been definitely identified as being of bacterial origin.

The other principal diagnosis in this study was AIECB. Although the majority of physicians include antibacterial agents as part of their treatment regimens for AIECB, the need for such agents has been questioned (Kronsick, 1991). Bacterial pathogens were identified in 34/59 (58%) of clinically-evaluable AIECB azithromycin group patients and 26/57 (46%) of patients who received co-amoxiclav in the present study. The pathogens were eradicated in all except one co-amoxiclav-treated patient and satisfactory clinical responses were attained in 93% of patients in both groups. Patients with AIECB tended to be older (mean ages 62.4 and 64.5 years in the azithromycin and co-amoxiclav groups, respectively) than those with acute bronchitis (mean ages 52.9 and 47.8 years, respectively) and thus the condition is potentially more serious. In view of the good clinical responses achieved, this study strongly supports the role of antibacterial agents in the treatment of AIECB. Another problem frequently encountered in older patients is their poor compliance to therapy, particularly if the regimen involves multiple doses each day over a period of more than 7 days. A complete course of azithromycin lasts only 3 days, and thus there is an increased likelihood of the patient adhering to the regimen.

In conclusion, this large-scale study provides further evidence that a once-daily, 3-day azithromycin regimen is as effective as co-amoxiclav three times daily for 10 days in patients with a range of acute lower respiratory tract infections.

Acknowledgements

The active participation of the other members of the Azithromycin Study Group is gratefully acknowledged: Drs J. Lyons and P. O’Flaherty (Borrisokane); Drs M. Cranfield and R. Baldwin (Gwent); Drs P. Quinn and A. Howard (Sligo); Drs B. Murray and J. Quirke (Clonakility); Drs B. Hamilton and P. G. Jones (Essex); Dr W. D. Carr (Fife); Dr M. McGinnity (Monaghan); Dr C. McNamara (Dublin); Dr C. Ryan (Killucan); Dr P. McDonagh (Galway), Dr D. J. Wheatcroft (Hertfordshire); Dr Y. Singh (Clywd); Dr M. Caraher (Monaghan); Dr M. D. Nightingale (Surrey); Dr D. Payler (Worcestershire); Dr E. Hartmen (Cavan); Dr F. Doig (Irvine); Dr L. McEntee (Trim); Dr P. Neary (Drogheda); Dr A. Bremner (Glasgow), Dr M. Kelly (Kilcullen), and Dr P. J. O’Brien (Galway).
References


Morandini, G., Perduca, M., Zannini, G., Foschino, M. P., Miraglia, G. & Carnimeo, N. S.


